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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/823,317

04/13/2004

Wilfried M. Braje

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WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
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EXAMINER

BERNHARDT, EMILY B

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/823,317

Applicant(s)

BRAJE ET AL.

Examiner

Emily Bernhardt

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 and 26-28 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-23 and 26-28 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1/24/05.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: REQUEST FOR INFORMATION.

REQUEST FOR INFORMATION

Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application.

In the specification on p.3 applicants have stated the reason for the proviso excluding two compounds from the claims. The examiner requests the following:

1) the earliest date the compound was available for sale; and 2) any published information relating to the excluded compound especially any information as to possession of activity and/or uses.

Additionally, the examiner requests any information pertaining to activity and/or uses for the compound listed in the CHEMCATS DATABASE filed in the IDS of 1/24/05 .


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571- 272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Emily Bernhardt
Primary Examiner
Art Unit 1624



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Claims 1-23,26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Nature of Q and Ar rings is not completely defined as only 2 atoms are positively recited as ring members. Thus the nature of remaining ring atoms is not clear. From the examples in the specification carbon atoms are remaining ring members. Note In re Wiggins 179 USPQ 421 regarding such terminology.

2. Phraseology excluding A's as all nitrogens and carbons and in claims 5 and 13 requires clarification since these variables are part of the "Q" ring which in main claim 1 must be **hetero**aromatic and can only have up to 2 N atoms not 3.

3. "Where appropriate..." appearing throughout the dependent claims is not clear as to what conditions the functional groups following this term can be present and when it is not appropriate. Perhaps "optionally" was intended?

7. In claim 12 the wording "R1 is different from hydrogen and methyl" is grammatically awkward. Does applicant mean "in which R1 is not hydrogen or methyl?"

8. Method claim 27 is of indeterminate scope as no particular disorder is ever recited. Such claim language reciting a particular mode of action(s) may read on

diseases that are affected by dopamine binding in ways not yet understood. What distinguishes a mammal, the apparent host, in need of such treatment vs. one who is not in need? D3 receptors recited may be involved in all diseases so how can one be sure that any use of claim's 1 scope does not infringe these claims ?

Additionally, determining whether a given disease responds to D3 receptor agonists or antagonists would involve much experimentation since a negative response from one patient does not mean the drug isn't useful as no drug has 100% effectiveness. Thus what "success rate" determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, par. two is whether applicants have clearly defined "their" invention **not** what may be discovered by future research as this type of claim language clearly requires.

Claims 8 and 19 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 8 permits A2 as N which is not included within 6 from which 8 depends. In claim 19 phenyl is recited for Ar which is not included in claim 13.

Claims 1-23 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Q as pyridyl, pyrimidyl and Ar as phenyl and R2 as alkyl, does not reasonably provide enablement for the varying scope of azines permitted at both Q and Ar as well as fused piperazines at R1/R2 and at any pair of R2. For the latter, specification is silent as to the availability of necessary reactants needed to prepare such ring systems or if they are commercially available. Note In re Howarth 210 USPQ 689; Ex parte Moersch 104 USPQ 122 for the need to show starting material sources commensurate with the instant scope. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. There is no basis in the prior art for such a variety of rings, ring systems all known to be selective D3 receptor ligands. Compounds actually made and tested are much closer to each other than to remaining scope exemplifying the rings at Q and Ar indicated above. Only one example of a bicyclo ring, namely, the 2,5 diazabicyclo[2.2.1]heptane ring system has been made and tested vs. what is claimed at R2/R1 or at R2's at any location. There is thus no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they

are so structurally dissimilar as to be chemically non-equivalent and no exemplary test data has been provided for such a scope. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition which such factors such as:

1) Breadth of the claims- the claims cover compounds easily in the millions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature as it involves binding to dopamine (D3) receptors. It is well established that “the scope of enablement varies inversely with the degree of unpredictability of the factors involved” and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18. A range of K_i values is reported which is enormous- covering $\leq 1\mu\text{M}$ to $.04\text{nM}$ - a 25000 fold spread;

3) Direction or guidance- as stated above the compounds made are not representative of the instant scope but represent only a small fraction of what is being claimed;

4) State of the prior art- The compounds are both fused and unfused piperazine derivatives attached at one end to azines which in turn are substituted with an aromatic sulfonyl group by way of an amino, oxy or carbon link While such

compounds are known as evident from the art applied below, they are directed to compounds used in screening for other type of receptors or as reagents and thus do not evidence the many structural permutations permitted in the instant scope are known for at least one use in the prior art much less for the instant uses;

5) Working examples- While test data has been presented it is too homogeneous in terms of structural variation and there is thus no clear evaluation of which functional groups out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied. Claims 26-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating schizophrenia and Parkinson's Disease, does not reasonably provide enablement for treating any CNS disorder or kidney disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Remaining uses embraced which from a reading of the specification include memory, cognitive, sleep, eating disorders to name just a few, are not remotely enabled based on what is currently known in the art for dopamine receptors in particular D3 receptors relied on herein. Such uses

are not considered all treatable based simply on D3 receptor binding as evidenced by the references cited by applicants such as Schwartz, Dooley or Joyce.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Interchim Intermediates. The reference cited by applicants depicts a compound named therein which is embraced by the instant claim language. It appears to be part of a Chemical library used as synthetic reagents. Note the attached Request for Information.

Claims 1-3,10,11,23 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by Jones (WO'265). The WO publication cited by applicants is applied as of its international filing date which precedes applicants' US filing date. It describes several compounds within the claims' scope as part of a library used for screening binding at various receptors such as neuropeptides. See compounds appended to the Chemical abstract provided by the examiner. It describes

compounds within the instant scope when pyrazine is present corresponding to instant Q. It is recognized that applicants are claiming benefit under 35 USC 119(e) which date would antedate Jones. However, the provisional application is not in English and thus a certified copy is needed. Note for obtaining such a date there must be compliance with 35 USC 112 as is set forth in MPEP 706.02, section V, part (D).

Applicants' IDS filed 7/8/04 has been considered except for the last entry on p.2 as this article is not seen in the file. Also it is noted that the IDS appears to be 3 pages long but only first 2 pages are in the file. Once a copy is provided, a signed PTO 1449 copy will be forwarded to applicants. Remaining IDS statement is signed and forwarded with this action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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